

NOVEL ANTI-ARRHYTHMIC AND HEART FAILURE DRUGS THAT TARGET THE
LEAK IN THE RYANODINE RECEPTOR (RYR2) AND USES THEREOF

ABSTRACT OF THE DISCLOSURE

[00218] The present invention provides methods for limiting or preventing a decrease
5 in the level of RyR2-bound FKBP12.6 in a subject. The present invention further provides
methods for treating and preventing atrial and ventricular cardiac arrhythmias, heart failure,
and exercise-induced sudden cardiac death in a subject. Additionally, the present invention
provides use of JTV-519 in a method for limiting or preventing a decrease in the level of
RyR2-bound FKBP12.6 in a subject who has, or is a candidate for, atrial fibrillation. Also
10 provided are uses of 1,4-benzothiazepine derivatives in methods for treating and preventing
atrial and ventricular cardiac arrhythmias and heart failure in a subject, and for preventing
exercise-induced sudden cardiac death. The present invention also provides methods for
identifying agents for use in treating and preventing atrial fibrillation and heart failure, and
agents identified by these methods.

15